Author's response to reviews

Title: Cost-effectiveness of MRI compared to mammography for breast cancer screening in a high risk population

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To

Dr. Melissa Norton,

Editor-in-Chief, The BMC-series journals

Dear Dr Norton,

Thank you for considering our MS: 1543760476185532 titled “Cost-Effectiveness of MRI Compared to Mammography for Breast Cancer Screening in a High Risk Population” for publication in *BMC Health Services Research* journal; and thank you for giving us the opportunity to revise and resubmit the manuscript and address the reviewers’ comments. We have made substantial changes to the manuscript based on the useful comments by the reviewers.

Below is the point-by-point response to the reviewers’ comments. Once again, thank you for your time and consideration. We hope that you find this second revision of the manuscript acceptable for publication in the *BMC Health Services Research* journal.

Please contact me at (404) 778-5554 or at Christopher.Flowers@emoryhealthcare.org if you have any questions.

Regards,

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Response to Reviewer 1

1. The evaluation of Cost-effectiveness of MRI compared to mammography for screening women at high risk for breast cancer is of great interest, as this procedure is now more and more adopted in many western countries. Study methodology and analysis is accurate and the study gives interesting information to evaluate the impact and cost-effectiveness of screening high risk women with MRI.

We would like to thank the reviewer for the time spent to review our manuscript.
Response to comments raised by Reviewer 2

We appreciate your detailed and thoughtful comments on the revised version of our manuscript. We have attempted to address all your comments and suggestions. We hope that you find that we have addressed your comments adequately in the re-revised manuscript. Given below is the detailed point-wise response to your comments.

1. **Regarding the response to previous comment #4 and in regard to the sentence added by the authors: “Neither costs nor outcomes were discounted since costs and benefits all occurred within the year that resources were utilized and each strategy required the recurring costs of screening.”**: The Panel on Cost-Effectiveness in Health and Medicine recommends discounting of both costs and effects to account for the time in the future when costs and effects occur. If the model follows a 25 year old cohort for 40 years, it seems that by using a 0 discount rate, the authors suggest that payers should value the costs of treating cancer 40 years in the future the same as having to pay to treat a cancer today. It is important to properly discount costs and effects that occur differentially between strategies in future years back to present value.

We agree with the reviewer’s comment. In this second revision, we discount all costs and benefits at the rate of 5%. All results were revised to reflect this change and discounted and undiscounted values are described in ¶ 2 of page 9.

2. **Regarding previous comment #10, the model diagram is still quite confusing. Although the authors clarify this point in their response to reviewer comments, it is unclear from the diagram and legend itself that the model tracks each breast separately. A larger source of confusion is that the temporary health state of “False Positive” occurs for women with true node positive and node negative breast cancer. Positive test results for women with cancer would seem to be true positives. Finally, it is confusing to see the “false positive” temporary health state as a transition from screening back to the “no cancer” state.**

We appreciate the reviewer’s comment. Please note that in our model, each breast is tracked independently, however, the patient’s state is determined by occurrence or no occurrence of cancer in the first breast. We have modified Figure 1 and its legend accordingly. The temporary health state of “False Positive” in women with true node positive and node negative breast cancer occurs incases of false positive results for the other breast. The same explanation applies to the “false positive” temporary health state as a transition from screening back to the “no cancer” state.

3. **The ending sentence of the results and conclusions sections of the Abstract in**
which $50,000/QALY is used as a threshold and the conclusion is that MRI is not cost-effective at this time appear somewhat at odds with the first paragraphs of the discussion section: “In this model, MRI screening approaches cost-effectiveness if a threshold of $120,000/QALY is used.” My reading of the authors’ results is that even at $120,000/QALY, MRI does not appear particularly attractive being more costly and less effective 42% of the time.

We agree with your comment and have modified the sentence in the conclusion section of the abstract to read “Although breast MRI provides a net benefit when compared to mammographic screening for high risk women, it is not cost-effective even as the willingness to pay threshold approaches $120,000/QALY.”

4. Though requested in previous comment #3, no description of how the model outputs were compared to observational or SEER data for face validity has been provided. If no such comparisons have been made, please state this in the discussion as an important limitation when the reader evaluates the policy analysis based on the model.

In the revised version, we have now added this limitation in the Discussion section.

5. Regarding previous comment #8, it appears that the probabilities listed in the Tornado diagram do not match the table and also exceed 1.

We appreciate the reviewer’s comment and agree. The listed probabilities were errors and have been corrected in the Tornado diagram.

6. Table 3 shows a range for the utility of undergoing screening that exceeds 1.0 (undergoing screening is better than living in perfect health). Is this a mistake or a consequence of using normal approximations of binomial distributions in the probabilistic sensitivity analysis? If the latter, would using beta distributions for the probabilistic sensitivity analysis be more appropriate?

We appreciate the reviewer’s comment and agree. The listed range for the utility of undergoing screening in Table 3 was erroneous and has been corrected.